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Formulation and Evaluation of Perindopril Erbumine Gastro Retentive Raft Tablets

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Abstract: The study focuses on the formulation and evaluation of gastro retentive raft tablets of Perindopril, designed to enhance its bioavailability and therapeutic effects in managing hypertension. By employing a combination of hydrophilic polymers sodium alginate, pectin, HPMC K4M, and Carbopol 934, a buoyant raft system was developed that aims to prolong gastric retention and achieve controlled drug release. Various formulation parameters, including polymer type and concentration, were systematically evaluated. *In vitro* studies assessed, floating ability, raft strength and drug release kinetics of the raft tablets. Total of 9 formulations are developed and F9 results demonstrated that the formulated tablets exhibited favourable buoyancy and a sustained release profile, with drug release primarily driven by zero order and polymer swelling mechanisms.

Keywords: Raft systems, Perindopril direct compression, Raft forming, Floating drug delivery system

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Introduction

Oral route is most common preferred route of drug administration to systemic circulation. It offers number of advantages such as predictability, ease of dosing, patient compliance and flexibility in formulation (Venkata *et al.*, 2014). To overcome the limitations of immediate release, development of controlled release has come into existence to achieve the drug concentration in git for prolonged period of time (Venkata *et al.*, 2014). But the effect of controlled release dosage forms depends on gastric emptying, and gastric residence time of drug. Long residence time of drug is required for anti hypertensive anti-inflammatory agents. Gastro retentive drug delivery is alternative to those drugs required long residence time. Prolonged gastric residence time will increase bioavailabilty of drugs.

Prolonged gastric residence time can be attained by floating drug delivery that causes

buoyancy in gastric fluid, mucoadhesion, high density (sinking) systems that is retained in the bottom of the stomach. Of these raft systems are more advantages to release the drug for prolonged period of time (Pawar *et al*., 2015). A floating drug delivery system works by reducing the density of the medication, allowing it to float on the stomach's contents. This is typically achieved by incorporating alkaline substances like bicarbonate or carbonate and using ingredients that form a gel-like structure. The system, which relies on a "raft-forming" process, helps increase the bioavailability of the medication by ensuring it stays in the stomach longer. As a result, the drug has more time to be absorbed, leading to better effectiveness, especially for medications that need to be absorbed in the acidic environment of the stomach (Naresh and Niranjan, 2024).

The primary objective of RAFT-forming tablets is to maintain buoyancy in the gastric fluid. This is achieved through the incorporation of low-density materials and gas-generating agents, such as sodium bicarbonate, which produce carbon dioxide upon contact with gastric acids. The resultant buoyant tablet floats on the gastric contents, allowing for controlled and sustained drug release while minimizing the effects of gastric emptying.

Materials and Methods

The mechanism of raft formation in floating tablets begins when the tablet is ingested and enters the stomach. Upon contact with the stomach's acidic environment, the ingredients, such as alkaline bicarbonates or carbonates, react with the acid to produce carbon dioxide (CO_2) gas. At the same time, gel-forming agents within the tablet begin to absorb water and swell, forming a gel-like structure. This gel matrix traps the CO_2 gas, causing the tablet to expand and form a "raft" that floats on the surface of the stomach contents. The floating raft serves as a barrier, controlling the release of the drug and preventing it from quickly passing into the intestine. This prolonged stay in the stomach allows the drug to be absorbed more effectively by the stomach lining, ultimately improving the bioavailability of the medication. The process ensures a sustained release, providing a more consistent and controlled absorption, especially for drugs that require absorption in the acidic stomach environment (Naresh and Niranjan, 2024).

Preformulation Studies

(i) Perindropril solubility was determined in various solvents like water, 0.1 N HCl, and acetate buffer.

(ii) *Determination of UV spectrum of perindopril erbumine*: 10 mg of Perindopril erbumine was dissolved in 10 ml of buffers so as to get a stock solution of 1000 µg/ml concentration. From the above stock solution pipette out 1 ml of the solution and makeup the volume to 10ml using buffer to get the concentration of 100 µg/ml concentration. From this stock solution pipette out 1 ml of the solution and makeup the volume to 10 ml using buffer to get the concentration of 10 µg/ml concentration, this solution was scanned under UV Spectroscopy using 200-400 nm.

Preparation of Standard Calibration Curve of Perindopril erbumine at pH 1.2

(A) *Preparation of Stock Solution*: 10 mg of Perindopril erbumine was dissolved in 10 ml of pH 1.2 buffers so as to get a stock solution of 1000 µg/ml concentration.

(B) *Preparation Standard Solution*: 0.1 ml of stock solution was diluted to 10 ml with pH 1.2 buffer in 10 ml volumetric flask this gives a concentration of 10 µg/ml. Aliquot of standard drug solutions were prepared by withdrawing 0.5, 1, 1.5, 2, 2.5 and 3 ml transferred into 10 ml volumetric flask and were diluted up to the mark with pH 1.2 buffer. This gives the final concentration of 5-30 µg/ml of Perindopril erbumine, respectively. The absorbance of the solution was measured against pH 1.2 as blank using UV visible spectrophotometer at 210 nm. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

FTIR: The IR spectra of Perindopril and the

Table 1: Formulation table

Ingredients (mg)	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
DRUG	8	8	8	8	8	8	8	8	8
Sodium Alginate	37.5	75	112.5	- - -	- - -	- - -	112.5	-	56.25
Pectin	-	-	-	37.5	75	112.5	—	112.5	56.25
HPMC K15M	25	25	25	25	25	25	-	-	-
Xanthan gum	-	-	-	-	-	-	25	-	-
Carbopol 940	-	-	-	-	-	-	-	25	25
Calcium carbonate	15	15	15	15	15	15	15	15	15
Sodium bicarbonate	35	35	35	35	35	35	35	35	35
PVP K30	20	20	20	20	20	20	20	20	20
M.C.C	94.5	57	19.5	94.5	57	19.5	19.5	19.5	19.5
Ethyl cellulose	10	10	10	10	10	10	10	10	10
Mg. stearate	3	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2	2
TOTAL	250	250	250	250	250	250	250	250	250

Perindopril-excipient mixture were obtained using a FTIR- spectrophotometer through the KBr Pellet technique. The scanning was carried out within the wave range of 400 to 4000 cm^{-1}.

Preparation of raft Tablets: Raft forming perindopril erbumine tablets were prepared by direct compression method using variable concentrations of different polymers (Table 1). Direct compression method is a widely employed method.

Direct Compression

In this process the tablets are compressed directly from powder blends of active ingredient and suitable excipients, which will flow uniformly into the die cavity and form a firm compact. The ingredients were passed through a 40 µm mesh during the preparation of granules. The components were blended in batches, with magnesium stearate and talc added at the final stage of mixing. This mixture was then subjected to an evaluation of pre-compression parameters, including angle of repose, bulk density, tap density, Carr's index, and Hausner's ratio. The mixture was compressed into tablets using 10 mm flat punches on a Rimek mini press 16-station rotary compression machine. Each tablet weighed 250 mg, containing 8 mg of Perindopril erbumine. After compression, the tablets were tested for weight variation, thickness, friability, hardness, *in vitro* disintegration time, and dissolution time.

Evaluation of precompression parameters

Precompression Parameters (*Moganti and Shivakumar, 2021*):

(A) *Bulk Density* (*BD*): It is the ratio of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of powder was carefully poured into graduated measuring cylinder through large funnel and volume was measured which is called initial bulk volume. Bulk density is expressed in g/cc and is given by:

$$BD = M / Vo$$

Where, Db = Bulk density (g/cc); M is the mass of powder (g); Vo is the bulk volume of powder (cc).

(B) *Tapped density* (*TD*) (*Mandal et al., 2016*): Ten grams of powder was introduced into a clean, dry 100 ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and tapped volume was read. It is expressed in g/cc and is given by:

$$TD = M / Vt$$

Where, Dt = Tapped density (g/cc); M is themass of powder (g); Vt is the tapped volume of powder (cc).

(C) *Compressibility index*: The compressibility of the powder was determined by the Carr's compressibility index (Table 2).

Carr's Index (%) = tapped density - bulk density/tapped density x 100

(D) *Hausner ratio* (*Wannasarit et al., 2020*): It is calculated as:

Hausner ratio = tapped density/bulk density

Values of Hausner ratio: < 1.25: good flow; >1.25: poor flow. If the Hausner ratio is between 1.25-1.5, flow can be improved by addition of glidants.

(E) *Angle of repose* (*θ*): It is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. Fixed funnel method was used (Table 3). A funnel was fixed with its tip at a given height (h), above a flat horizontal surface on which a graph paper was placed. Powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of funnel. The angle of repose was then calculated using the formula:

$$\tan \theta = h / r$$

$$\theta = \tan^{-1} (h/r)$$

Where, θ = angle of repose h = height of pile, r = radius of the base of the pile.

Evaluation of Tablet properties

(a) *Thickness and diameter* (*Wannasarit et al., 2020*): Control of physical dimension of the tablet such as thickness and diameter is essential for consumer acceptance and tablet uniformity. The thickness and diameter of the tablet was measured using Vernier calipers. It is expressed in mm.

(b) *Hardness*: The Mansanto hardness tester was used to determine the tablet hardness. The tablet was held between a fixed and moving jaw. Scale was adjusted to zero; load was gradually increased until the tablet fractured. The value of the load at that point gives a measure of hardness of the tablet. Hardness is expressed in Kg/cm^2.

(c) *Friability* (*F*): Tablet strength was tested by Friabilator USP EF-2. Pre weighed tablets were allowed for 100 revolutions (4 min), taken out and were dedusted.

The percentage weight loss was calculated by rewriting the tablets. Tablets of friabilities under 1% are acceptable. The % friability was calculated by:

$$F = WA-WB/WA *100$$

Where, F--Friability, WA-- Initial weight (g), WB-- Final weight (g).

(d) *Weight variation test* (Singh *et al.*, 2018): The weight of the tablet being made is routinely measured to ensure that a tablet contains the proper amount of drug. The USP weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average. The tablet

Table 2: Relation between the Carr's index of powder and its flow characteristics

S. No.	Carr's index	Type of flow
1	5-15	Excellent
2	12-15	Good
3	18-21	Fair
4	23-30	Poor
5	33-38	Very poor
6	40	Extremely poor

meet the USP test if not more than 2 tablets are outside the percentage limits and if no tablets differs by more than 2 times the percentage limit. USP official limits of percentage deviation of tablet are presented in Table 4.

$$PD=(W_{Avg}-W_{Initial}/W_{Avg)} *100$$

Where, PD = Percentage deviation, W avg = Average weight of tablet, W initial = individual weight of tablet.

(e) *Uniformity of drug content*: Five tablets of various formulations were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in buffers, the drug content was determined using a UV/Visible Spectrophotometer (PG Instruments) at 210nm.

(f) *In vitro buoyancy studies*: The *in vitro* buoyancy was determined by floating lag time and total floating time as per the method described by Roy and Shahiwala (2009). The tablets (n = 3) were placed in 1000 ml of 0.01 N HCl in USP type II dissolution apparatus (37 ± 0.5°C, 50 rpm). The time required for the tablets to rise to the surface and float was determined as floating lag time. The duration of time the dosage form constantly remained on the surface was determined as the total floating time.

(g) *In vitro release study* (*Patel and Patel, 2013*):

Procedure:

Apparatus	USP XXIV dissolution testing apparatus II (paddle method)
Dissolution medium	pH 1.2 acidic buffer
Temperature	37± 0.5 °C
RPM	50
Vol. withdrawn and replaced	5 ml every 1 h
λ max	210 nm in pH 1.2
Blank solution	Buffers used
Duration of study	24 h
Volume of dissolution media	900 ml

The release rate of Perindopril erbumine from tablets was determined using the United States Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle type).The dissolution test was performed using 900 ml of pH 1.2 for 24 h at 37.5±0.5 0 C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly for 24 h, and the samples were replaced with fresh dissolution medium. The samples diluted to a suitable concentration with

Table 3: Comparison between angles of reposes and flow property

Angle of Repose	Flow
<25	Excellent
25 – 30	Good
30 – 40	Moderate
>40	Poor

Table 4: Weight variation limits

S. No.	Average weight of tablet (mg)	Maximum % difference allowed
1	130 Or less	10
2	130-324	7.5
3	324 or more	5

Table 5: Solubility profile of Perindopril erbumine in different solvents

S. No.	Media	Solubility (mg/ml)
1	Water	0.919
2	0.1 N HCl (pH 1.2)	0.684
3	4.5 pH acetate buffer	0.412
4	pH 6.8	0.340
5	pH 7.4	0.326

respected dissolution medium. Absorbance of these solutions was measured at 210 nm using a UV-Visible Spectrophotometer (Instruments). Percentage of drug release was calculated.

(h) *Raft strength measurement*: To measure the raft strength using an in-house method, an amount of tablet powder corresponding to a single dose was dissolved in 150 ml of 0.1N HCl. This mixture was kept at a temperature of 37°C in a 250 ml glass beaker. During the entire process (30 min), a wire probe (L-shaped, with a diameter of 1.2 mm) was positioned upright in the beaker to allow the raft to form around it. The strength of the raft was measured by the modified balance method. Water was slowly added drop by drop to a pan until the raft broke, and the total amount of water required to break the raft was recorded (Rajmane *et al.*, 2022).

Results and Discussion

Preformulation studies

(a) *Solubility studies*: Perindopril was freely soluble in distilled water and 0.1N HCl after solubility determination (Table 5, Fig. 1).

(b) *Standard calibration curve of Perindopril Erbumine*: λmax was found to be at 210 nm, so the calibration curve of Perindopril erbumine was developed at this wave length. The calibration

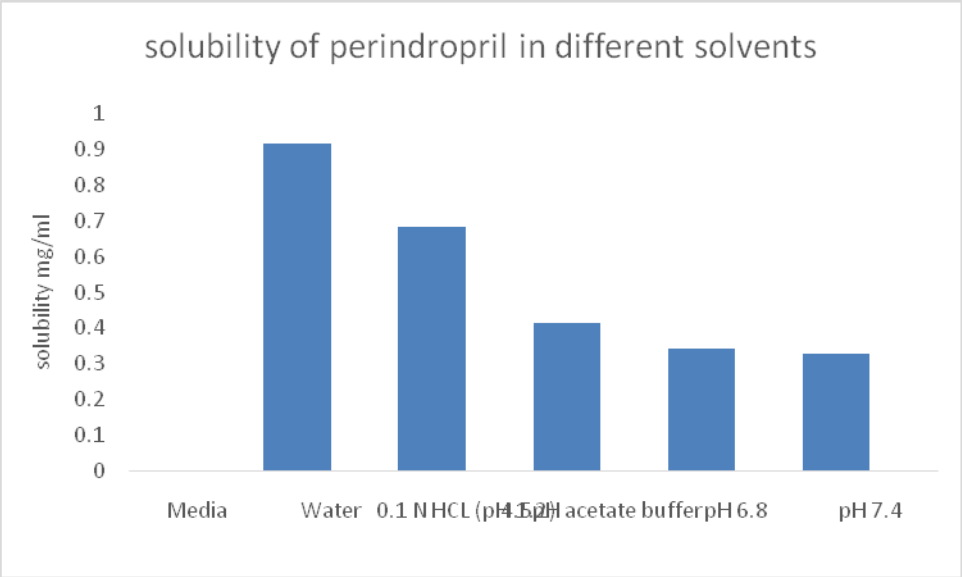

Fig. 1: Solubility profile of Perindopril erbumine in different solvents.

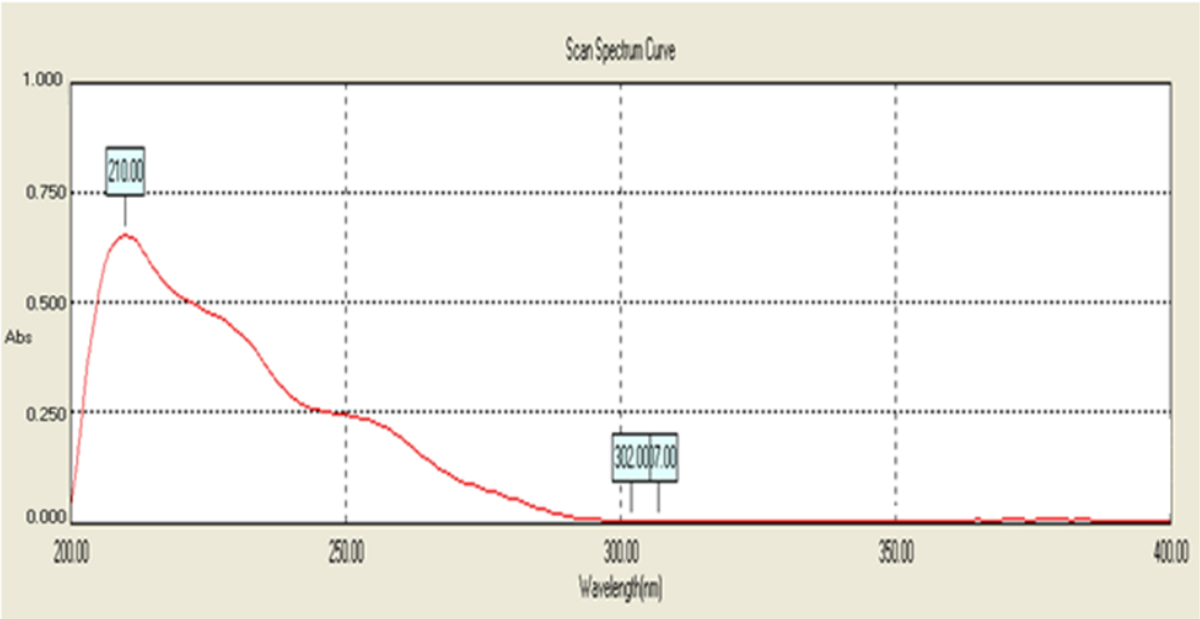

Fig. 2: λmax of Perindopril Erbumine.

curve showed linearity between 5-35 µg/ml concentration ranges. The standard calibration curve of Perindopril erbumine was determined in O.1N HCl pH 1.2 by plotting absorbance against concentration at 210 nm. The r^2 value was found to be 0.999. The calibration curve is presented in Figure 2.

Calibration curve:

Absorbance data for the calibration curve of Perindopril erbumine in 0.1N HCl is depicted in Table 6 and Figure 3.

Identification of Pure Drug

FT-IR spectroscopy was used to determine the functional group present in the pure drug sample.The characteristic peaks were observed at 2941.14cm-1 corresponding to N-H stretching, 1893.93cm^{-1}, corresponding to C=O stretching, 1443.20 corresponding to CH3, 1482.48 cm^{-1}

Table 6; Absorbance data for the calibration curve of Perindopril erbumine in 0.1N HCl

Concentration (µg/ml)	Absorbance
0	0
5	0.124±0.014
10	0.246±0.016
15	0.374±0.042
20	0.488±0.014
25	0.634±0.016
30	0.749±0.024

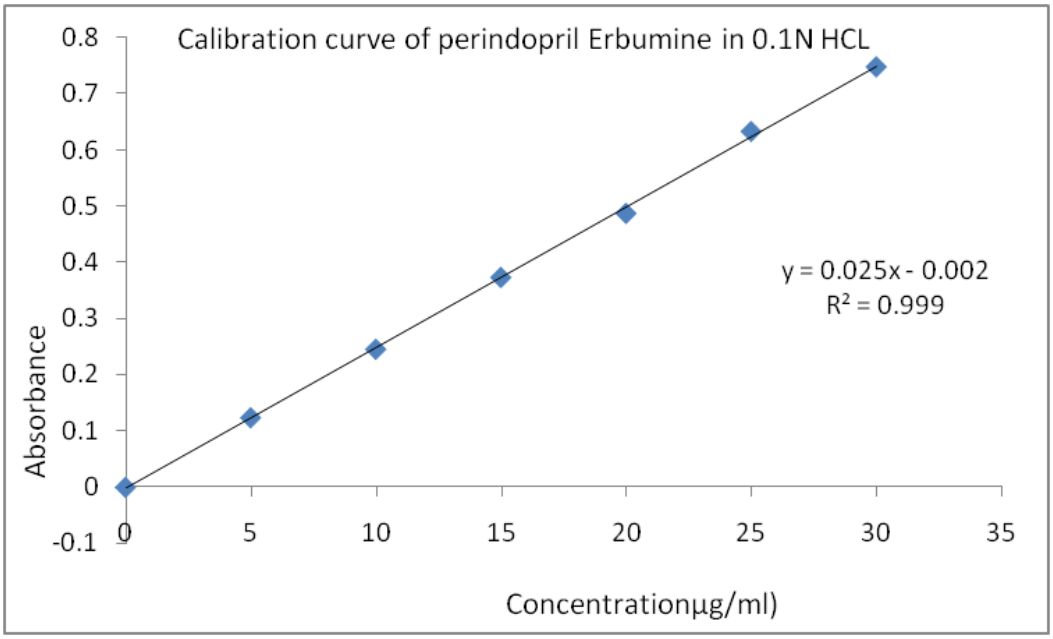

Fig. 3: Standard calibration curve of Perindopril erbumine in 0.1N HCl.

corresponding to C=C stretching. IR SPECTRA of Perindopril is shown in Table 7 and Figures 4, 5.

From the compatibility studies it was concluded that the functional groups that were presented in the pure drug were present in the Excipients blend with very minute changes, from this we can conclude that the drug and excipients have no interactions.

Evaluation of preliminary characteristics of Perindopril erbumine

The initial batches were assessed based on key post-compression properties, including weight uniformity, friability, hardness, and *in vitro* disintegration. The results of these evaluations are summarized in Table 8.

Raw materials and prepared powder blend of all formulations were evaluated for their flow properties such as the angle of repose, bulk density, tapped bulk density, Hausner's ratio and Carr's index. The Carr'sindex, Hausner's ratio and angle of repose ranged between 1153±.26 to 14.81 ±1.28; 1.12±0.29 to 1.17±0.04; and 24.25±0.68 to 30.68, respectively. It could be concluded from the result that the powder blend with different formulations components were having good flow properties, good compressibility, which allow

Table 7: FTIR Interpretation

Functional groups	Stretching/ Deformation	Pure drug (cm^{-1})	Drug+Excipients (cm^{-1})
N=H	Stretching	2941.14	2929.15
C=O	Stretching	1893.93	1790.57
C=C	Stretching	1482.48	1424.85
CH3	Deformation	1443.20	1438.14
O-H	Stretching	3002.88	3004.94

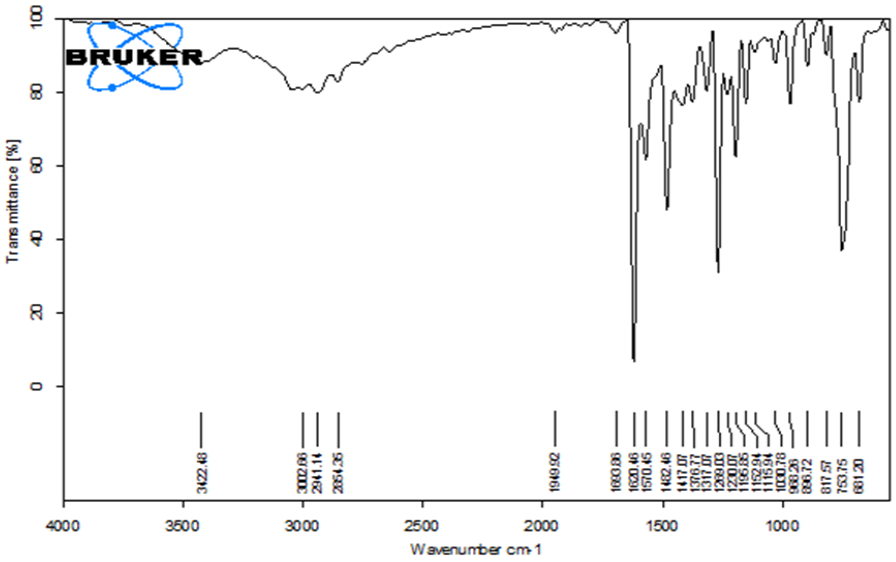

Fig. 4: IR spectra of Perindopril erbumine.

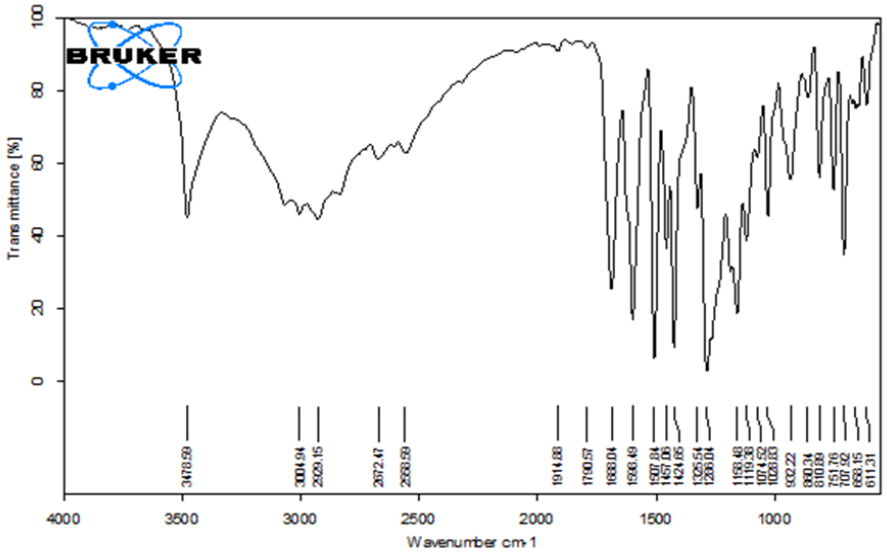

Fig. 5: FT-IR Spectra of Perindopril erbumine and Excipients.

Table 8: Pre-compression parameters of Perindopril erbumine floating tablets

FC	Derived properties		Flow properties		
	Bulk density (mean±SD)	Tapped density (mean±SD)	Angle of repose (mean±SD)	Carr's index (mean±SD)	Hausner's ratio (mean±SD)
F1	0.48±0.06	0.56±0.015	26.38±0.30	14.28±0.02	1.16±0.06
F2	0.46±0.04	0.52±0.02	27.42±0.39	11.53±0.26	1.13±0.03
F3	0.42±0.04	0.48±0.01	24.02±0.68	12.58±2.08	1.14±0.05
F4	0.46±0.02	0.54±0.015	26.26±0.96	14.81±1.28	1.12±0.29
F5	0.52±0.62	0.60±0.03	30.68±0.73	13.33±1.86	1.17±0.04
F6	0.49±0.28	0.58±0.006	29.26±0.36	15.51±0.22	1.18±0.35
F7	0.42±0.08	0.48±0.04	24.02±0.68	12.58±0.08	1.14±0.05
F8	0.52±0.12	0.60±0.03	30.68±0.73	13.33±0.86	1.17±0.04
F9	0.42±0.06	0.48±0.01	24.02±0.52	12.58±.08	1.14±1.05

Table 9: Post-compression evaluation of Perindopril erbumine floating tablets

Formulation Code	Avg. Wt (mg)	Hardness (kg/cm²)	Thickness (mm)	Friability (%)	Drug content (%)
F1	239.12±0.58	5.34±0.42	3.41±0.10	0.21±0.46	97.21±1.02
F2	238.97±0.26	5.32±0.04	3.49±0.04	0.41±0.79	95.64±0.46
F3	240.56±0.10	5.30±0.02	3.82±0.04	0.74±0.56	98.72±0.22
F4	241.56±0.48	5.28±0.16	3.55±0.06	0.54±0.42	94.12±067
F5	240.23±0.56	5.33±0.07	3.36±0.24	0.63±0.18	96.02±0.48
F6	239.78±0.22	5.45±0.10	3.54±0.10	0.70±0.39	98.54±0.16
F7	241.89±0.18	5.36±0.02	3.40±0.12	0.19±0.86	91.22±0.28
F8	239.55±0.47	6.58±0.04	3.42±0.04	0.35±0.54	94.26±0.52
F9	239.41±0.42	6.24±0.02	3.54±0.06	0.48±0.12	97.54±0.44

these formulations to be directly compressed into tablets. The results are shown in Table 9.

Post compression evaluation of Perindopril erbumine floating tablets

The prepared floating tablets of Perindropril were evaluated for various post compression parameters like, average weight, thickness, hardness, friability, buoyancy parameters and drug content. The results are shown in Table 9. All values are expressed as mean ± SD (n=5).

In vitro drug release data of Perindopril erbumine floating raft tablets

Perindopril erbumine tablet test conditions for the dissolution rate studies were used according USP specifications using USP 24, type II apparatus. The dissolution medium was 900 ml of 0.1N Phosphate buffer. The temperature of the dissolution medium and the rate of agitation were maintained at 37±0.5°C and 50 rpm, respectively. Aliquots of 5 ml of the dissolution medium were

Table 10: *In vitro* drug release data of Perindopril erbumine floating tablets of Batch F1 to F9

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	52.92 ±0.78	36.07± 0.59	24.61± 0.26	59.46± 0.4	49.82± 0.74	32.21± 0.33	12.81± 0.14	12.81± 0.14	9.62± 0.14
2	67.47 ±1.40	50.81± 0.68	35.67± 0.78	64.32± 0.16	59.21± 0.36	46.59± 0.76	23.24± 0.36	23.24± 0.36	19.24± 0.36
4	86.18 ±0.28	71.23± 0.40	49.59± 0.22	79.21± 0.58	68.21± 0.58	52.36± 0.58	37.06± 0.48	37.06± 0.48	30.06± 0.48
6	96.46 ±0.69	88.52± 0.11	55.93± 0.49	86.21± 0.42	79.68± 0.44	69.94± 0.46	45.74± 0.63	45.74± 0.63	42.12± 0.12
8	99.23 ±0.85	92.08± 0.32	73.46± 0.36	90.21± 0.22	83.41± 0.26	78.42± 0.85	56.86± 0.24	59.97± 0.36	51.89± 0.72
10		98.18± 0.76	83.4± 0.48	98.45± 0.19	92.41± 0.14	85.23± 0.44	66.41± 0.49	66.37± 0.94	64.25± 0.29
12		100.26± 0.41	92.35± 0.10		99.96± 0.28	91.96± 0.96	78.22± 0.58	72.47± 0.10	76.11± 0.54
16			96.26± 0.76			96.21± 0.46	86.28± 0.12	80.28± 0.01	82.97± 0.22
18						98.59± 0.22	99.23± 0.10	85.86± 0.25	89.46± 0.16
20								91.12± 0.36	96.296± 0.52
24								95.36± 0.24	99.22± 0.27

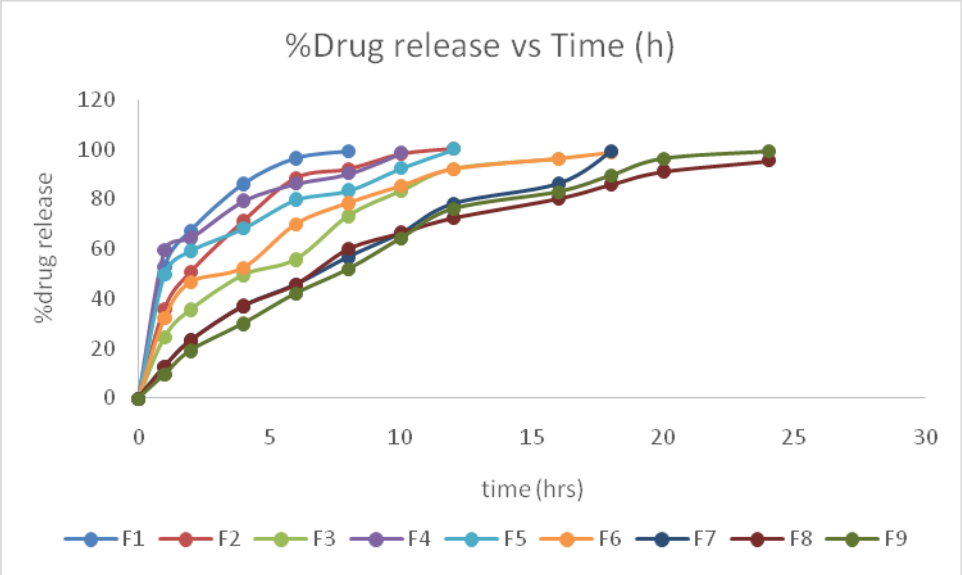

Fig. 6: *In vitro* drug release of formulation 1 to 9.

withdrawn at specific time intervals and the volume replaced by fresh dissolution medium, pre-warmed at 37±0.5°C. The drug concentration was determined spectrophotometrically at 210 nm using UV spectrophotometer (Shimadzu 1800). Formulation F9 showed maximum release at end of 24 h indication use of sodium alginate, pectin along with carbopol 934 developed a buoyant raft system that aims to prolong gastric retention and achieve controlled drug release. F9 follow zero order kinetics and mechanism of release is non-fickian diffusion. The *in vitro* drug

Table 11: Buoyancy study results

Formulation code	Floating Lag Time (sec)	Total Floating Time(h)
F1	78±0.02	>6
F2	67±0.48	>8
F3	58±0.22	>11
F4	60±0.47	> 8
F5	54±0.52	>10
F6	49±0.36	>15
F7	62±0.44	>14
F8	69±0.21	>18
F9	64±0.16	>18

Fig. 7: Raft formation of F9.

Table 12: Raft strength measurement

Formulation Code	Raft strength (g)
F1	2±0.14
F2	5±0.26
F3	8±0.19
F4	3±0.15
F5	6±0.06
F6	8±0.14
F7	2±0.28
F8	9±0.16
F9	9±0.04

release were shown in Table 10 and Figure 6.

Buoyancy studies

All the formulation showed good buoyancy parameters, floating lag time was found to be 49±0.36 to 78±0.02 sec and total floating time was between 6 to 18 h. The formulations containing carbopol 934 showed good buoyancy parameters when compared to formulations containing HPMC15KM. Among all the formulation F9 showed better result (Table 11).

In vitro buoyancy studies were conducted using tablets prepared by the effervescent method, employing sodium bicarbonate as a gas-releasing agent. When the tablets come into contact with the dissolution medium (0.01 N HCl), sodium bicarbonate generates carbon dioxide. This gas is trapped within the gel matrix formed by the hydration of the polymer, leading to a reduction in the tablet's density. As the tablet's density decreases below 1 g/ml, it becomes buoyant and floats in the dissolution medium.

In vitro Raft Strength measurement

Raft Strength of batches of Perindropril floating tablet F1-F9 was measured by in house method. Values are shown in Table 12, among that formulation F8 was found showing higher

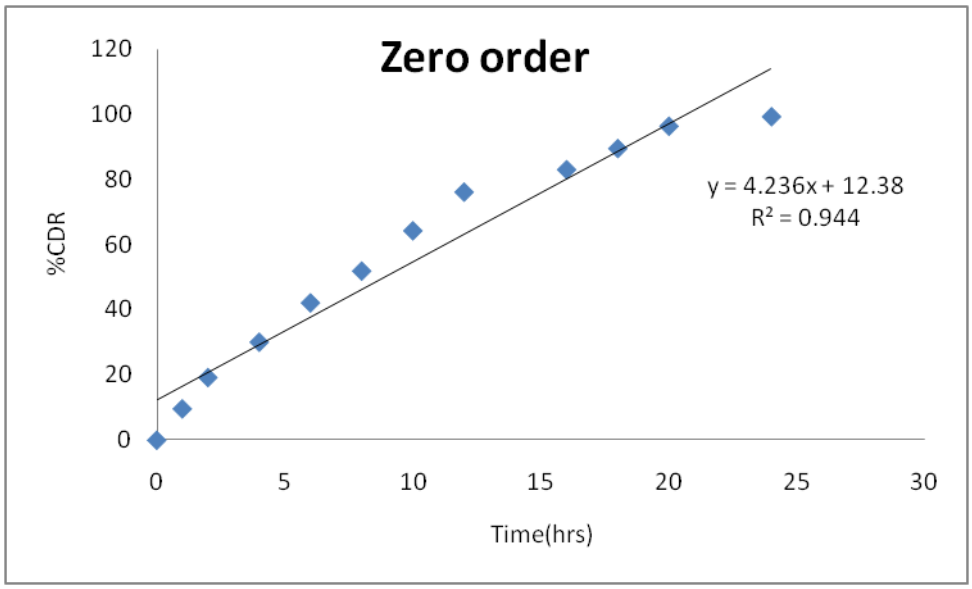

Fig. 8: zero order release kinetics of F9.

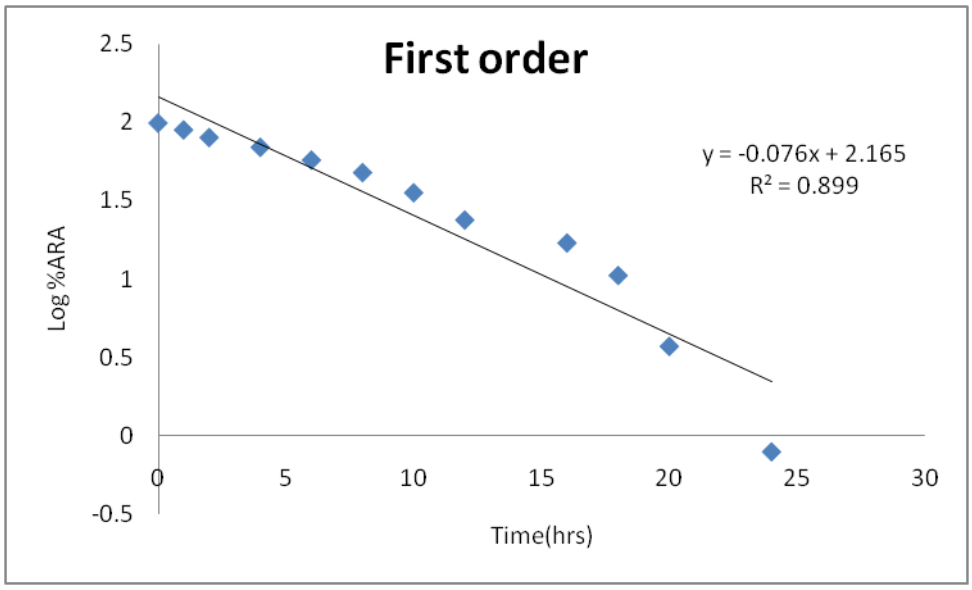

Fig. 9: First order release kinetics of F9.

strength i.e. 9±0.16 g.

Kinetics of Drug Release (*Singh et al., 2018*)

In determination of mechanism and kinetics of drug release, the results of the *in vitro* drug release study were fitted into various kinetic equations like zero order (cumulative per cent drug released versus time; Fig. 8), first order (log cumulative per cent drug retained versus time; Fig. 9), Higuchi (cumulative per cent released versus $\sqrt{T}$; Fig. 10), and Peppas (log of cumulative per cent drug released versus log time; Fig. 11). The kinetic model that best fits the dissolution data was evaluated by comparing the coefficient of determination (r^2 values obtained in various models; Table 13). In the Peppas (Fickian diffusion) model, mechanisms of drug release are characterized using the release exponent ("*n*" value). An "*n*" value of 1 corresponds to zero-order release kinetics (case II transport); 0.5 <*n*< 1

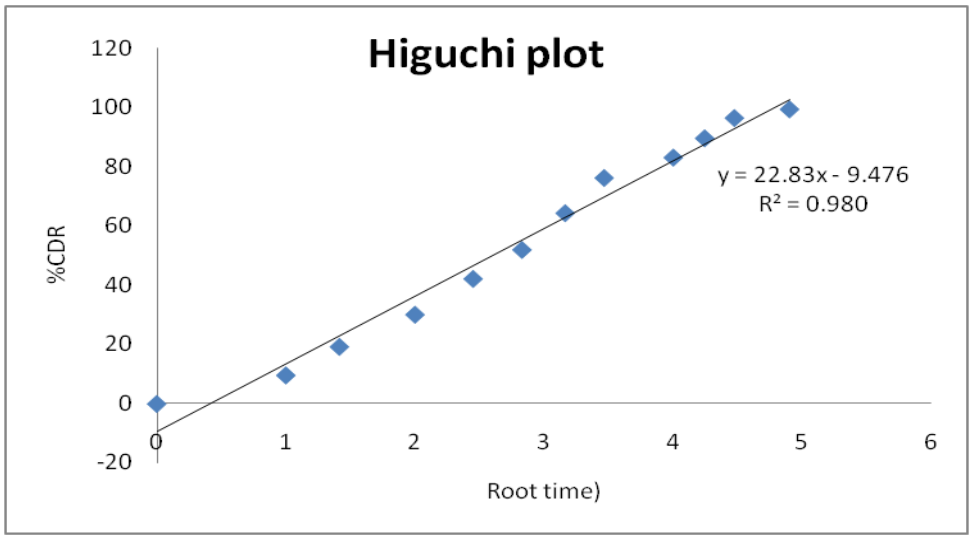

Fig. 10: Higuchi plot of F9.

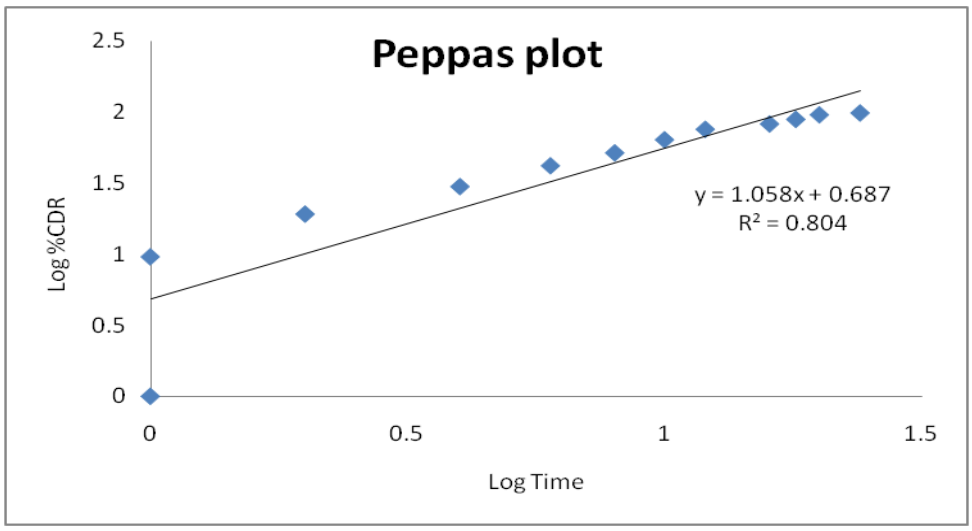

Fig. 11: Peppas plot of F9.

Table13: Kinetic release data of F9

Formulation	Correlation Coefficient (r2) Values				
	Zero order	First order	Higuchi's	Peppas's	
				R²	N
F9	0.944	0.899	0.98	0.8	1.0

means an anomalous (non-Fickian) diffusion release model; $n = 0.5$ indicates Fickian diffusion, and $n>1$ indicates a super case II transport relaxational release.

Conclusion

The floating raft tablets of perindopril are developed by direct compression. Preformulation studies indicate that there is no interaction between drug and polymers.All formulations were evaluated for physicochemical properties and result was found within the limit. Among all the formulation F9 showed better buoyancy and drug release profile. The release of drug from the

prepared formulations was found to follow zero order and mechanism was non-fickian. *In vitro* dissolution revealed that drug release rate was increased as the concentration of polymer decreased. Carbopol 934 showed greater drug release rate as compared to HPMC K15M.

Ethical Statement

No animal or microbes have been used or sacrificed for this study, hence Ethical Approval not required.

Author Contributions

Each author has contributed equally in designing the research, conducting thorough analysis, drafting the manuscript, and refining its content. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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